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Terms	Documents
T adj cell near5 (inhib$ or decrea$ or reduc$) and L2	58

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

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DATE: Tuesday, March 19, 2002 Printable Copy Create Case

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	DB=USPT; PLUR=NO; OP=ADJ		
L3	T adj cell near5 (inhib$ or decrea$ or reduc$) and L2	58	L3
L2	(FKBK or cyclospo$) near5 (muta$ or chang$ or delet$ or addit$)	258	L2
L1	mutat$ near5 macrol$ adj bindi$ adj prot$	0	L1

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L3: Entry 2 of 58 File: USPT Mar 5, 2002

DOCUMENT-IDENTIFIER: US 6352830 B1
TITLE: NF-AT polypeptides and polynucleotides and screening methods for immunosuppressive agents

Brief Summary Paragraph Right (10):
Putative intracellular receptors for FK506 and CsA have been described and found to be cis-trans prolyl isomerases (Fischer & Bang (1985) Biochim. Biophys. Acta 828: 39; Fischer et al. Nature 337: 476; Handschumacher et al. (1984) Science 226: 544; Lang & Schmid (1988) Nature 331: 453; Standaert et al. (1990) Nature 346: 671). Binding of the drugs inhibits isomerase activity; however, studies with other prolyl isomerase inhibitors (Bierer et al. (1990) Science 250: 556) and analysis of cyclosporin-resistant mutants in yeast suggest that the prevention of T lymphocyte activation results from formation of an inhibitory complex involving the drug and the isomerase (Bierer et al. (1990) Proc. Natl. Acad. Sci. U.S.A. 87: 9231; Tropschug et al. (1989) Nature 342: 953), and not from inhibition of the isomerase activity per se.

Detailed Description Paragraph Right (11):
The terms "candidate immunosuppressant" and "candidate immunosuppressant agent" are used herein interchangeably to refer to an agent which is identified by one or more screening method(s) of the invention as a putative inhibitor of T cell activation. Some candidate immunosuppressants may have therapeutic potential.

Detailed Description Paragraph Right (49):
Additional embodiments directed to modulation of T cell activation include methods that employ specific antisense polynucleotides complementary to all or part of the sequences shown in FIG. 12. Such complementary antisense polynucleotides may include nucleotide substitutions, additions, deletions, or transpositions, so long as specific hybridization to the relevant target sequence corresponding to FIG. 12 is retained as a functional property of the polynucleotide. Complementary antisense polynucleotides include soluble antisense RNA or DNA oligonucleotides which can hybridize specifically to NF-AT.sub.c mRNA species and prevent transcription of the mRNA species and/or translation of the encoded polypeptide (Ching et al. (1989) Proc. Natl. Acad. Sci. U.S.A. 86:10006; Broder et al. (1990)Ann. Int. Med. 113: 604; Loreau et al. (1990) FEBS Letters 274: 53; Holcenberg et al., WO91/11535; U.S. Ser. No. 07/530,165; WO91/09865; WO91/04753; WO90/13641; and EP 386563, each of which is incorporated herein by reference). The antisense polynucleotides therefore inhibit production of NF-AT.sub.c polypeptides. Since NF-AT.sub.c protein expression is associated with T lymphocyte activation, antisense polynucleotides that prevent transcription and/or translation of mRNA corresponding to NF-AT.sub.c polypeptides may inhibit T cell activation and/or reverse the activated phenotype of T cells. Compositions containing a therapeutically effective dosage of NF-AT.sub.c antisense polynucleotides may be administered for treatment of immune diseases, including lymphocytic leukemias, and for inhibition of transplant rejection reactions, if desired. Antisense polynucleotides of various lengths may be produced, although such antisense polynucleotides typically comprise a sequence of about at least 25 consecutive nucleotides which are substantially identical to a naturally-occurring NF-AT.sub.c polynucleotide sequence, and typically which are identical to a sequence shown in FIG. 12.

Other Reference Publication (11):
Emmel, E. et al. "Cyclosporin A specifically inhibits function of nuclear proteins involved in T cell activation", Science346:1617-1620 (1989).